

Remarks

Claims 1- 24 have been canceled previously or herein without prejudice or disclaimer. Applicants reserve the right to file one or more continuation applications directed to the subject matter encompassed by all canceled claims. Applicants submit herewith a Supplemental Application Datasheet (ADS) to amend the inventive entity to coincide with the currently claimed subject matter. Additionally, to comply with PTO guidelines the Domestic Priority Information section of the Supplemental ADS has also been amended to use the phrase "An application claiming the benefit under 35 USC 119(e)" in place of the former phrase "Non-provisional of".

Claims 25-74 are pending. No new matter has been added.

Formal Matters

Oath/Declaration

The Examiner stated that "[a] new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required." *See*, Paper No. 112804, page 3. More specifically, it was alleged that a new oath or declaration is required because "[n]on-initialed and/or non-dated alterations have been made to the oath or declaration...see page 19 of the Declaration." *See id.*

Applicants respectfully disagree. Initially, Applicants refer the Examiner to copies of the executed Declaration (3 pages in 4 counterparts, 12 pages total) and the executed return receipt card submitted herewith, which were submitted on the filing date of the present application. Applicants point out, and the return receipt verifies, that the Declaration is only 12 pages total and therefore could not possibly contain non-initialed and/or non-dated alterations on page 19. Furthermore, Applicants note that the Declaration as filed does not contain non-initialed and/or non-dated alterations on any of the 12 pages as filed. Thus, Applicants submit that the Declaration as previously filed is in full compliance and submission of a new oath or declaration is not required. Applicants respectfully note that the Examiner may have mistakenly included the Assignment as part of the Declaration as one of the previously submitted pages of the Assignment contains an alteration in the margin. This alteration, however, does not affect or alter the Declaration in the present application. ✓

Therefore, Applicants respectfully request the Examiner to withdraw the request for a new oath or Declaration.

Amendment of Inventorship

Applicants respectfully request consideration and entry of the present amendment to correct inventorship pursuant to 37 C.F.R. §1.48(b) (*Non-provisional application - fewer inventors due to amendment or cancellation of claims*). The presently pending claims are directed to HWBFY57 protein embodiments. In this regard, the undersigned has been informed that the inventive entity of the subject matter encompassed by the claims is: Steven M. Ruben, Craig A. Rosen, and Kimberly A. Florence. Accordingly, Applicants request that the presently pending application be amended to show the above three persons as inventors. Thus, please remove the following names from the list of inventors: Reinhard Ebner, Henrik S. Olsen, Yanggu Shi, Paul A. Moore, Daniel R. Soppet, and David W. LaFleur, Paul Young, George Komatsoulis, and Jian Ni.

Rejections under 35 U.S.C. §112, second paragraph

Claims 11 and 12 were rejected under 35 U.S.C. §112, first paragraph. Claims 11 and 12 have been canceled. Therefore, this rejection is now moot.

Rejection of Claims 11, 12, and 25-74 under 35 U.S.C. §§101 and 112, first paragraph

Claims 11, 12 and 25-74 were rejected under 35 U.S.C. § 101 for alleged lack of a specific and substantial utility or a well-established utility. *See*, Paper No. 112804, page 4. In particular, the Examiner indicated:

[t]he instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into the potential practical uses of the claimed nucleic acids.

See Id. at 6, first full paragraph.

Preliminarily, Applicants point out that claims 11 and 12 have been canceled herein without prejudice or disclaimer. Therefore, the rejection of these claims has been rendered moot.

As to the remaining rejected claims, Applicants respectfully disagree and traverse.

Contrary to the Examiner's allegations, the specification includes statements that provide specific, substantial, and credible asserted. In particular, the specification discloses that the HWBFY57 protein may be used as an agent for the treatment and diagnosis of specific "immunological disorders including, arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, sepsis, acne, and psoriasis." *See*, page 32, lines 26-29. The disclosed asserted utility is based on the combined teachings of the specification concerning: (1) homology between HWBFY57 and two members of the immunoglobulin (Ig) superfamily, CMRF-35 antigen and PIGR-1; (2) shared structural features to type Ia membrane proteins; and (3) HWBFY57 expression in cells of lymphoid origin.

Initially, the specification teaches, "[t]he translation product of this gene shares homology with CMRF-35 antigen...which is thought to be important as a cell membrane antigen present on the surface of monocytes, neutrophils, a proportion of peripheral blood T and B lymphocytes and lymphocytic cell lines." *See*, page 30, lines 27-32; *see also*, Green *et al.*, *International Immunology* (1998) 10:891-899 (submitted herewith and listed in the IDS as reference AE). Further, the specification teaches, "[t]he translation product of this gene also shares sequence homology with PIGR-1 protein...which is a member of the Immunoglobulin (Ig) superfamily." *See*, page 31, lines 1-3. The disclosed homology between these two Ig superfamily members would be significant to a person of skill in the art since it was well known that members of the Ig superfamily share conserved regions which, in fact, contribute to their overall functions.

Accordingly, Applicants respectfully direct the attention of the Examiner to the sequence alignment (submitted herewith as Exhibit A) between the HWBFY57 protein and the CMRF-35 and PIGR-1 sequences. The alignment reveals that the HWBFY57 protein shares 28% and 22% identity to CMRF-35 and PIGR-1, respectively. More importantly, however, the protein sequence of the HWBFY57 reveals that the protein contains three conserved regions which are typical of Ig superfamily members. Specifically, the HWBFY57 protein contains an Ig-like extracellular domain at about amino acid position 20-156, "a transmembrane domain at about amino acid position 157-173," and "a cytoplasmic tail encompassing amino acids 174-290" and containing immunoreceptor tyrosine-based inhibitory motifs (ITIM). *See*, specification, page 31, lines 20-25. Thus, Applicants contend

that one of skill in the art would appreciate the importance of these conserved regions and their contribution in the development and presentation of many human immunological diseases and disorders.

Furthermore, the specification also teaches that HWBFY57 is expressed in eosinophils, dendritic cells, and monocytes. *See*, page 32, lines 14-15. Applicants note that as of the filing date of the present invention it was well known that these cells play a significant role in immune responses. Thus, given the teachings in the specification that the HWBFY57 protein is a membrane associated protein expressed in cells of lymphoid origin and the conserved structural features of the Ig superfamily, particularly the ITIMs in the cytoplasmic region, the specification clearly and specifically asserts a biological role for the protein HWBFY57 of the present invention, *i.e.*, in the diagnosis and treatment of specific immunological disorders.

Applicants assert that the post filing publication Sui *et al.*, in fact, supports Applicant's asserted utility by confirming that other skilled artisans would not doubt or question that the HWBFY57 protein would be useful in the treatment and/or diagnosis of immune disorders. *See* Sui *et al.*, *Biochemical and Biophysical Research Communications* (2004) 319:920-928 (currently submitted herewith as reference AF in an IDS). Initially, Sui *et al.* identifies "a novel inhibitory receptor of immunoglobulin superfamily (IgSF), IgSF member 13 (IgSF13)...from human dendritic cells (DC). *See*, Sui *et al.* (2004), abstract. A sequence alignment, submitted herewith as Exhibit B, reveals that the IgSF13 polypeptide of HWBFY57 and the Sui *et al.* sequence share greater than 98% identity.

Furthermore, Sui *et al.* disclose that IgSF13 "is a type I transmembrane protein containing an N-terminal signal peptide, a extracellular region with a single Ig V-like domain, a transmembrane region, and a cytoplasmic tail with two classical immunoreceptor tyrosine-based inhibitory motifs (ITIM), suggesting its inhibitory function." *Id.* Next, Sui *et al.* disclose that "IgSF13 was selectively expressed in monocytes and monocyte related cells." *Id.* at 924, column 2.

Finally, Sui *et al.* confirms Applicant's asserted relevance of the homology of the present invention to CMRF35 and PIGR-1 in assigning use of the HWBFY57 protein for immune disorders. In particular, Sui *et al.* state that the primary sequence of "IgSF13 shows significant homology to human CMRF35 and pIgR" and that the IgSF13 "Ig-like domain was

also significantly homologous to that of human CMRF35 (44% identity) [and the] V4 domain of human PIGR-1.” *Id.* at page 923; *see also* Figure 1, pages 922-923. Based on the homology to CMRF-35 and other IgSF inhibitory receptors and the monocyte-related expression pattern, Sui *et al.* conclude that IgSF13 “might serve as an inhibitory receptor to negatively regulate the maturation/differentiation of immune cells.” *See, Id.* at 926-927. Thus, Sui *et al.* corroborates Applicant’s asserted utility in the treatment and diagnosis of immune related disorders and proves that one of skill in the art would not doubt the credibility of the asserted utility.

Notwithstanding the above, the specification asserts an additional specific, substantial, and credible utility for the presently claimed protein for use in identifying and/or targeting immune cells. *See*, specification page 33, lines 3-4. In particular the specification describes the HWBFY57 protein as a transmembrane protein expressed in eosinophils, monocytes, and dendritic cells. *See Id.* at 31, lines 20-24; and page 32, lines 19-21. The specification also teaches that “[p]rotein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.” *Id.* at 33, lines 3-4. Therefore, in view of the HWBFY57 tissue specific expression profile, and the high level of skill in the art as of the effective priority date, one of skill in the art would appreciate the use of the protein as an immunotherapy target for antibodies in order to treat immune system disorders, *e.g.*, rheumatoid arthritis and leukemia, associated with immune cells.

Applicants note that targeted therapeutics that deplete an entire class of cells displaying a particular epitope, such as CD20 expressing B cells (Maloney *et al.*, *Blood*, Vol. 84, No.8, pp. 2457-2466 (October 15, 1994) (currently submitted herewith as reference AG)), or CD4+ T cells (van der Lubbe *et al.*, *J. Autoimmunity*, Vol 10, pp. 87-97 (1997) (currently submitted herewith as reference AH)), were known in the art as of the effective priority date of the present application.

Moreover, other successful therapeutics have been developed against cell surface antigens for which the function is or was unknown. For example, Rituximab (manufactured by Genentech under the name RITUXAN[®]) is a monoclonal antibody that binds specifically the CD20 surface antigen found on both healthy and diseased B-cells. Rituximab is used for the treatment of patients with B-cell non-Hodgkin's lymphoma. *See*, O’Neal, *Clin. J. Oncol. Nursing*, 5(2):75-76 (2001) (currently submitted herewith as reference AI). Rituximab was

developed as an effective treatment for inducing cell death and sensitizing cells to chemotherapy, even though the function of CD-20 was not known. See, e.g., Riley *et al.*, *Semin Oncol.* (27)6-12:17-24 (2000), abstract (currently submitted herewith as reference AJ).

Similar to the cell surface expression of CD20 in B-cells, it is known that the HWBFY protein is expressed on the surface of immune cells. Thus, the HWBFY57 protein would be useful for targeting cytotoxic agents to immune cells, for example, for the treatment and/or diagnosis of immune disorders such as, for example, rheumatoid arthritis and leukemia.

Applicants submit that, for the reasons stated above, the utility asserted in the specification for HWBFY57 protein is indeed *specific, substantial and credible*. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 101 be reconsidered and withdrawn.

For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, the claimed invention is supported by a specific, substantial and credible asserted utility. The Examiner “should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a ‘lack of utility’ basis unless a 35 U.S.C. § 101 rejection is proper.” M.P.E.P. § 2107 (IV) at 2100-36. Therefore, because the claimed invention complies with the utility requirement of 35 U.S.C. § 101, the rejections under 35 U.S.C. § 112, first paragraph, based on the alleged lack of utility of the claimed invention, should be withdrawn. See, Paper No. 112804, page 6, second full paragraph. Accordingly, Applicants respectfully request that the rejection of claims 25-74 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Rejections under 35 U.S.C. §112, first paragraph

Claims 11, 12 and 25-74 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement because the “Applicant has not provided sufficient guidance as to how to make and use the encoded polypeptides which are not 100% identical to the polypeptide of SEQ ID NO:65, but which still retain a desired property of the polypeptide of SEQ ID NO:65.” See Paper No. 112804, page 6, last paragraph. More specifically, it is asserted that:

Due to the large quantity of experimentation necessary to generate the infinite number of variant[s] recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding

which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art...and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

See id. at page 9, first full paragraph.

Preliminarily, Applicants point out that claims 11 and 12 have been previously cancelled, thereby rendering their rejection under 35 U.S.C. § 112, first paragraph, moot. With respect to remaining claims 25-74, Applicants disagree and traverse.

Applicants respectfully submit that the proper legal standard for evaluating enablement is whether “the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied.” *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970). The Federal Circuit has held that making the claimed species and screening them for function is acceptable, as long as the experimentation is not undue. The test is whether it would require undue experimentation to practice the invention – even when a claim might encompass some inoperative embodiments. *See Atlas Powder v. E.I. Du Pont de Nemours & Co.* 750 F.2d 1569, 224 U.S.P.Q. (BNA) 409 (Fed. Cir. 1984). Therefore, it is clearly not *per se* undue to make and test variants within the scope of the claims, particularly when specific guidance was clearly disclosed in the specification coupled with what was known in the art at the time the invention was filed.

The present application presents a situation similar to that described in *In re Wands*, where the specification was found enabling for the claimed antibodies because of the considerable direction and guidance in the specification, the high level of skill in the art, and the well-established methods used to practice the invention. As discussed below, the present specification, like *In re Wands*, provides more than ample guidance to those of ordinary skill in the art for how to make and use the claimed polypeptides.

At the time the invention was filed, it was routine to determine empirically whether particular variants of a protein have either the biological activity or the antigenicity of the parent protein. Furthermore, the specification describes and teaches uses of the claimed variants that do not require retention of biological activity, for example, as an immunogen to

produce antibodies against the claimed polypeptide. *See* page 100, lines 22-30. Additionally, the specification teaches four preferred immunogenic epitopes of SEQ ID NO:65 which contribute to the biological activity or antigenicity of the HWBFY57 protein. *See* page 32, lines 9-13.

Accordingly, one skilled in the art, enlightened by the teachings of the present application (particularly, for example, the sequence of HWBFY57), could readily envision each polypeptide sequence that comprises the specified polypeptides. For example, the skilled artisan could clearly envision each of the polypeptides that are at least 90% or 95% identical to the polypeptide of SEQ ID NO:65 as a polypeptide with, *e.g.*, 1-10 conservative amino acid substitutions within a segment of 100 contiguous amino acids. Indeed, nothing more than a basic knowledge of the genetic code and what is described in the specification would be required for the skilled artisan to identify every single polypeptide that is at least 90% or 95% identical to the amino acid sequence of SEQ ID NO:65. Clearly, such knowledge is well within the common knowledge of the skilled artisan. Further, the instant claims do not require the claimed sequences to possess any particular activity or characteristic beyond the described sequence, and the subject matter of what is claimed is fully supported by the specification.

Moreover, it is well-established that a “gene is a chemical compound, albeit a complex one”. *Amgen, Inc. v. Chugai Pharmaceutical Co., LTD.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). Thus, the claims of the instant application, directed to, for example, polynucleotides encoding polypeptides that are at least 95% identical to the amino acid sequence of the disclosed SEQ ID NO:65 (or of the polypeptide encoded by the cDNA of the claimed deposit), are essentially chemical claims involving generic chemical formulas. As stated in *Regents of the University of California v. Eli Lilly & Co.*, (119 F.3d 1559, 1569, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997)), “In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass.” All of the objectives met by a generic chemical formula are similarly met by the explicit description in the instant specification of both a polynucleotide and polypeptide sequence (*i.e.*, SEQ ID NOs:19 and 65) and claims to polypeptides that are 90% or 95% identical over the full length of the amino acids of that sequence. Likewise, the

‘generic chemical formula’ put forth in the instant specification (*i.e.*, SEQ ID NOs:19 and 65) also allows the skilled artisan to identify polynucleotide sequences complementary to SEQ ID NOs:19 and 65, polynucleotides encoding fusion proteins comprising SEQ ID NO:65, *etc.* That is, the instant claims clearly distinguish the boundaries of each claimed genus and identify all of the members of each genus.

Thus, armed with the disclosure in the specification and what was known in the art at the time the instant application was filed, one of skill in the art could readily envision, make and screen the claimed polypeptide variants, and then use these variants that share the biological activity or the antigenicity of the parent protein. Therefore, a patent application disclosure that contains a teaching of how to make and use the invention must be taken as enabling unless the Patent Office provides sufficient reason to doubt the accuracy of the disclosure. *In re Marzocchi*, 439 F.2d. 220, 223-224, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971).

In view of the foregoing, Applicants submit that the claims fully meet the enablement requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection to claims 25-74 be reconsidered and withdrawn.

Rejections under 35 U.S.C. §112, first paragraph

Claims 11, 12 and 25-74 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly “containing subject matter which was not [sufficiently] described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.” *See*, Paper No. 112804, page 9, penultimate paragraph. In particular, it was asserted that:

[t]he instant claims are not directed to that which is disclosed as essential to the invention...Thus, with the exception of the polypeptide of SEQ ID NO: 65, the skilled artisan cannot envision encompassed variants. Therefore, only a polypeptide of SEQ ID NO: 65, and polypeptides consisting of fragments thereof, or polypeptides consisting of fragments thereof and heterologous sequences (e.g. carrier or tag sequences), but not the full breath of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

See id. at paragraph spanning pages 10-11.

Applicants respectfully disagree and traverse. Applicants submit that one skilled in the art would reasonably envision and conclude that Applicants had possession of the polypeptides encompassed by the rejected claims. Applicants respectfully submit that the Examiner has underestimated the teaching of the present application and the level of skill in the art on the priority date of the present application.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02.

The Federal Circuit has re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed,'" *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000). Further, the Federal Circuit has also emphasized the importance of what the person of ordinary skill in the art would understand from reading the specification; and not whether the specific embodiments had been explicitly described or exemplified. Indeed, the court noted, "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d at 1001, (emphasis added).

Applicants submit that the specification describes with reasonable clarity that the inventors were in possession of a limited genera of claimed variants to SEQ ID NO:65 on the priority date of the present application. The specification explicitly states, for example, at page 100, lines 17-26 that the invention includes polypeptide variants (e.g., 5-10 substitutions, deletions, or additions) of the polypeptide of SEQ ID NO:65 or the polypeptide encoded by the cDNA contained in the deposited clone. The specification also provides the skilled artisan with the detailed structure of the novel protein of the invention. *See* sequence listing, SEQ ID NO:65, pages 38-39. Accordingly, one of ordinary skill in the art, enlightened by the specification and provided with, for example, the polypeptide sequence of SEQ ID NO:65, could readily envision any number of polypeptide variants that would comprise, for example, 5-10 substitutions, deletions, or additions as compared to the amino

acids of the reference polypeptide sequence. Therefore, the description of the species is representative of the claimed genus and the specification clearly conveys that Applicants were in possession of the claimed invention on the priority date of the instant application.

Furthermore, once one of ordinary skill in the art is given the complete polypeptide sequence shown in SEQ ID NO:65, the skilled artisan could readily envision any number of polypeptides comprising a polypeptide sequence which is 90 or 95% identical to the polypeptide sequence of SEQ ID NO:65. The specification clearly teaches, for example at page 98, line 21 to page 100, line 16 how to make and then determine a polypeptide variant that is 90% or 95% identical to the HWBFY57 amino acid sequence. Applicants note that the level of skill in the art on the priority date of the present application was very high. Accordingly, one skilled in the art, enlightened by teachings of the present application and of the amino acid sequence of the SEQ ID NO:65, could readily envision polypeptide sequences that comprise the specified polypeptides.

Thus, from reading the specification, the skilled person would immediately recognize that, at the time the specification was filed, the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563). Therefore, the specification contains an adequate written description of the claimed polypeptides.

The Examiner has cited *University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997) (hereinafter "*Eli Lilly*") in making the assertion that the disclosure of the single isolated polypeptide sequence SEQ ID NO:65 "is not sufficient to describe the essentially limitless genera encompassed by the claims." See Paper No. 112804, page 10, first full paragraph. Applicants assert that under *Eli Lilly*, there is adequate written description for the instant claims.

The claims at issue in *Eli Lilly* were directed to genetic material using "generic statement[s]" such as "vertebrate insulin cDNA" or "mammalian insulin cDNA." *Lilly*, 119 F.3d at 1568. The Federal Circuit found that these statements were not an adequate description of the genus because the claims described the gene only by what the gene did (functional description), and "did not define any structural features commonly possessed by the members of the genus" such that one skilled in the art could "visualize or recognize the identity of the members of the genus." *Id.* In order to satisfy the written description requirement, then, the court held that:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

Id. at 1569 (emphasis added).

Thus, the Federal Circuit indicated that the written description requirement for generic claims to genetic material, such as cDNA, may be satisfied by: 1) providing the sequences of a representative number of nucleic acids which fall within the scope of the genus; or 2) by providing a recitation of structural features common to a substantial portion of the members of the genus. Applicants assert that, to the satisfaction of the second test set forth in *Eli Lilly*, the description of the reference polypeptide SEQ ID NO:65 provides one skilled in the art with the necessary recitation of structural features common to members of the genus, which features “constitute a substantial portion of the genus.” *Id.* The recitation of the structural features of the reference protein is a recitation of the structural features common to the members of the genus because the proteins included within the genus will have, for example 5-10 variations in their amino acid sequence and/or 90% or 95% of their amino acid sequence (primary structure) in common to the reference polypeptide of SEQ ID NO:65.

As discussed above, once one of ordinary skill in the art is enlightened by the specification and provided with, for example, the reference polypeptide sequence of SEQ ID NO:65, the skilled artisan could readily envision any number of polypeptide variants that would comprise the amino acids of the reference polypeptide sequence and any number of polypeptides comprising a polypeptide sequence which is 90% or 95 % identical to the polypeptide sequence of SEQ ID NO:65. Therefore, the description of the species is representative of the claimed genus and the specification clearly conveys that Applicants were in possession of the claimed invention on the priority date of the instant application.

For all of the above reasons, Applicants respectfully assert the subject matter of the claims was sufficiently described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Therefore, under the applicable case law, claims 25-74 fully satisfy the written description requirement of 35 U.S.C. 112, first paragraph. Thus,

Applicants respectfully request that the Examiner reconsider and withdraw of the rejection of claims 25-74 under 35 U.S.C. § 112, first paragraph.

Rejections of Claims 11 and 12 under 35 U.S.C. §102

Rejection under 35 U.S.C. §102(b)

Claims 11 and 12 were rejected under 35 U.S.C. §102(b). Claims 11 and 12 have been canceled. Therefore, this rejection is now moot.

Rejections under 35 U.S.C. §102(e)

Claims 11 and 12 were rejected under 35 U.S.C. §102(b). Claims 11 and 12 have been canceled. Therefore, this rejection is now moot.

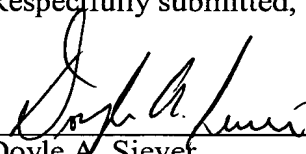
Conclusion

Applicants respectfully request that the above-made amendments and remarks be entered and made of record in the file history of the instant application. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425.

Respectfully submitted,

Date: 4/1/2005


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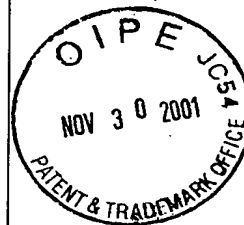
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RETURN RECEIPT CARD

(MPEP § 503)

OIPE:

Please Date Stamp In The
Box Below And Return To
Addressee



Application of: Soppet et al.

Attorney Docket No.: PZ037P1C1

Application Serial No.: Unassigned

Art Unit: Unassigned

Filed: Herewith

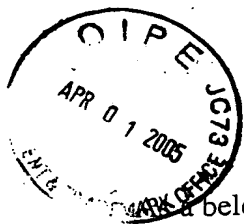
Examiner: Unassigned

Title: 33 Human Secreted Proteins

**The following documents were filed by Human Genome Sciences, Inc.
via hand delivery on November 30, 2001:**

1. Return Receipt Card;
2. Serial Number Postcard;
3. Fee Transmittal with appropriate fee(s) (in duplicate);
4. Utility Patent Application Transmittal;
5. Application Data Sheet (8 pages);
6. Specification: 347 pages Description; 5 pages [24] Claims; 1 page Abstract;
7. Sequence Listing in paper form (94 pages);
8. Request Under 37 C.F.R. § 1.821(e);
9. Preliminary Amendment (3 pages);
10. Version With Markings to Show Changes Made;
11. Statement Under 37 C.F.R. § 3.73, Revocation of Prior Powers of Attorney or Authorizations of Agent, and Power of Attorney or Authorization of Agent (3 pages);
12. Copy of executed Declaration in prior Application No. 09/628,508 (3 pages in 4 counterparts) (12 pages);
13. Copy of executed Assignment in prior Application No. 09/628,508 (2 pages in 4 counterparts) (8 pages); and
14. Copy of Petition for Extension of Time in prior Application No. 09/628,508.

KKH/JMM/CAW/ba



DECLARATION FOR PATENT APPLICATION

I, the below named inventor, I declare that I believe I am an original, first and joint inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled:

33 HUMAN SECRETED PROTEINS

the specification of which was filed on **July 28, 2000** as Application Serial No. **09/628,508**.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 C.F.R. § 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT international application, which designated at least one country other than the United States listed below, and have also identified below any foreign application for patent or inventor's certificate, or PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s):

<u>Priority Claimed</u>	
Yes	No

(Number)

(Country)

(Day/Month/Year Filed)

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below.

60/119,468
(Application Serial No.)

10 February 1999
(Filing Date)

I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s), or under § 365(b) of any PCT international application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose information that is material to patentability as defined in 37 C.F.R. § 1.56 that became available between the filing date of the prior application and the national or PCT international filing date of this application.

PCT/US00/03062
(Application Serial No.)

8 February 2000
(Filing Date)

Pending
(Status: patented, pending, abandoned)

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: James H. Davis (Reg. No. 40,582), Kenley Hoover (Reg. No. 40,302), Joseph Kenny (Reg. No. 43,710), Jonathan L. Klein (Reg. No. 41,119), and Michele Wales (Reg. No. 43,975) of Human Genome Sciences, Inc. 9410 Key West Avenue, Rockville, Maryland, 20878.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of first joint inventor: Daniel R. Soppet

Inventor's signature: _____ Date: _____
Residence: 15050 Stillfield Place, Centreville, VA 22020 Citizenship: US
Post Office Address: same as above

Full name of additional joint inventor: Paul A. Moore

Inventor's signature: _____ Date: _____
Residence: 19005 Leatherbark Drive, Germantown, MD 20874 Citizenship: UK
Post Office Address: same as above

Full name of additional joint inventor: Yanggu Shi

Inventor's signature: _____ Date: _____
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Post Office Address: same as above

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Inventor's signature:  Date: 10/05/00

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Inventor's signature: _____ Date: _____

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Full name of additional joint inventor: Jian Ni

Inventor's signature: _____ Date: _____

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DECLARATION FOR PATENT APPLICATION

As a below named inventor, I declare that I believe I am an original, first and joint inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled:

33 HUMAN SECRETED PROTEINS

the specification of which was filed on **July 28, 2000** as Application Serial No. **09/628,508**.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 C.F.R. § 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT international application, which designated at least one country other than the United States listed below, and have also identified below any foreign application for patent or inventor's certificate, or PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s):

<u>Priority Claimed</u>	
Yes	No

(Number)

(Country)

(Day/Month/Year Filed)

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below.

60/119,468

(Application Serial No.)

10 February 1999

(Filing Date)

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PCT/US00/03062

(Application Serial No.)

8 February 2000

(Filing Date)

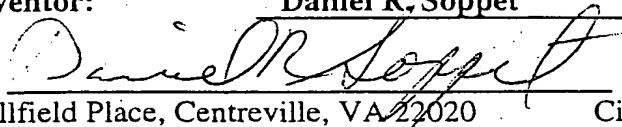
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Inventor's signature: 

Date: 10/6/00

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PCT/US00/03062
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Post Office Address: same as above

Full name of additional joint inventor: Reinhard Ebner

Inventor's signature: Reinhard Ebner Date: 10/10/05

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Post Office Address: same as above

Full name of additional joint inventor: Steven M. Ruben

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Residence: 18528 Heritage Hills Drive, Olney, MD 20832 Citizenship: US
Post Office Address: same as above

Full name of additional joint inventor: Craig A. Rosen

Inventor's signature: Craig A. Rosen Date: 10/16/00
Residence: 22400 Rolling Hills Road, Laytonsville, MD 20882 Citizenship: US
Post Office Address: same as above

Full name of additional joint inventor: David W. LaFleur

Inventor's signature: David W. LaFleur Date: 10/9/00
Residence: 3142 Quesada Street, N.W., Washington, DC 20015 Citizenship: US
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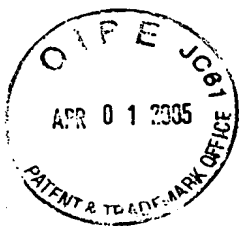
Inventor's signature: George A. Komatsoulis Date: 16 Oct 2000
Residence: 9518 Garwood Street, Silver Spring, MD 20901 Citizenship: US
Post Office Address: same as above

Full name of additional joint inventor: Jian Ni

Inventor's signature: _____ Date: 10/9/00
Residence: 5502 Manorfield Road, Rockville, MD 20853 Citizenship: CN
Post Office Address: same as above

		Signal Peptide	
HWBFY57	M-----P L L T L Y L L F W L S C Y S I A T Q I T G P T T V N G L E R		33
CMRF-35	M T A R A W A S W R S S A L L L L V P G Y --- F P L S H P M T V A G P V G		
PIGR-1	M-----L L F V L T C L L A V F P A I S T K S E I F C P E E V N S V E G		
HWBFY57	G S L T V Q C V Y -- R S G W E T Y L K W W C R - G A I W R D C K I L V K T S G		70
CMRF-35	G S L S V Q C R Y -- E K E H R I L N K F W C R - P P Q I L R C D K I V E I K G		
PIGR-1	N S V S I T G Y P P T S V N R H T R K Y W C R - Q G A R G G C I T I S S E G		
		Extracellular Region	
HWBFY57	S E Q E V K R D R V S I K D N O K N R L E T V T M E D I M K T D A D F Y W C G I		110
CMRF-35	S A G K - R N C R V S I R D S P A N L S E L V T L E N T E E D A C T Y W C G V		
PIGR-1	Y V S S K Y A G R A N L T N F E N G T E V V N I A Q L S Q D D S G R Y K C G L		
HWBFY57	E --- K T G N D L G V T V Q V T I D P A ---		128
CMRF-35	D T P W L R D F H D P I V E V E V S V F P A G T T T A S S P Q S S --- M G ---		
PIGR-1	G I N S R G L S F D - - V S L E V S Q G E G L L N D T K V Y T V D - - L G R T V		
HWBFY57	--- P V T Q E T S S S P T L T ---		150
CMRF-35	- T S G P T K L P V H T W P S V I R K D S P E P --- S P H P C S L F S N V R		
PIGR-1	T I N C P F K T E N A Q K R K S E Y K Q I G L Y P V L V I D S S G Y V N P N Y T		
		Transmembrane Region	
HWBFY57	K L L K L S V L - - L P L I E T - I X - L L L L V A A S L L A W R M M K Y Q Q K		186
CMRF-35	F L L L V L L E - - L P L L L S - M L G A V I W N R P O R S S R S R Q N W P K		
PIGR-1	G R I R I D I Q G T G Q L L E S V V I N Q I R I S D A G O Y L C Q A G D D S N S		
		ITIM	
HWBFY57	A A G M S P E Q V L Q L E G D I C Y A D I T L Q L - - A G T S P R K A T T K		223
CMRF-35	G E N Q - - - - -		
PIGR-1	N K K N A D L Q V E K E - E P E L V M E D L R G S V T F H C A L G P E V A N V A		
		Cytoplasmic Tail	
HWBFY57	L S S A Q V D Q V E V E Y V T M A S I P K E D I S Y A S L I T G A E D Q E P T Y		263
CMRF-35	-----		
PIGR-1	K F L C R Q S S G E N C D V V V N T I G K R A P A F E G R I I L N P Q D K D - -		
HWBFY57	C N M G X L S S X L P C R G P E P T E M S T I S R P - - - - -		290
CMRF-35	-----		
PIGR-1	--- C S F S V V I T C L R K E D A G R M L C G A H S D G Q L Q E G S P I Q A W		

Alignment of HWBFY57, CMRF-35 and PIGR-1 (Inhibitory receptors of IgSF). HWBFY57: Signal peptide: amino acids 1-19, extracellular region: amino acids 20-156, Transmembrane region: amino acids 157-173, Cytoplasmic tail: amino acids 174-290. ITIM is defined by the consensus sequence (S/I/L/V)xYxx(L/V) (See, Sui *et al.* (2004) page 920, second column; see also, Green *et al.*, *International Immunology*, (1998) 10:891-899 at Figure 3).



HWBFY57	MPLELLVYLLHLLHFWLSCYSLA	TOITGPTHTVNGLERGSLIVOCVWRSQWEHML	50
IgsF13	MPLELLVYLLHLLHFWLSCYSLH	VIQITGPTHTVNGLERGSLIVOCVWRSQWEHML	
HWBFY57	KWNGRGATWRDCKGLKLVKTS	SGSEOEVKRDRVSTKDNOKNRTPEVHMEIDLMK	100
IgsF13	KWNGRGATWRDCKGLKLVKTS	SGSEOEVKRDRVSTKDNOKNRTPEVHMEIDLMK	
HWBFY57	IDADTYWCGGHEKTCGNDE	LGVAIVOVTHDPAPVLOEHTSSSPTELTGHHHNDNRH	150
IgsF13	IDADTYWCGGHEKTCGNDE	LGVAIVOVTHDPAPVLOEHTSSSPTELTGHHHNDNRH	
HWBFY57	KLLKLSVLLPLFTFTX	GLLELVAAASLLAWRMKQCKKAAAGMSPEQVLOPLF	200
IgsF13	KLLKLSVLLPLFTFTX	GLLELVAAASLLAWRMKQCKKAAAGMSPEQVLOPLF	
HWBFY57	GDLCYADLTLLQAGTSP	PKATTKLESSAOVDQVEVENAVATMASLTPKEDTSVA	250
IgsF13	GDLCYADLTLLQAGTSP	PKATTKLESSAOVDQVEVENAVATMASLTPKEDTSVA	
HWBFY57	SLHTLGAEDDOEPPTYCNM	GLSSXILPGRGPEEPTEYSTISRP	290
IgsF13	SLHTLGAEDDOEPPTYCNM	GLSSXILPGRGPEEPTEYSTISRP	

Alignment of HWBFY57 and IgsF13